

# ONDANSETRON AND MEPERIDINE PREVENT POSTOPERATIVE SHIVERING AFTER GENERAL ANESTHESIA

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## Abstract

**Background:** Postoperative shivering is one of the common problems following general anesthesia and may lead to multiple complications. The aim of this study was to examine the preventive effects of Ondansetron and Meperidine on postoperative shivering.

**Methods:** This randomized placebo-controlled double blind clinical trial included 90 patients scheduled for elective gynecologic operations, randomly divided to three groups. Ondansetron (4mg), Meperidine (0.4 mg/kg) and 2 cc normal saline (as a control group) were administered immediately before the induction of anesthesia. Anesthesia induced equivalently for all. Patients were observed in terms of vital signs, side effects and shivering.

**Results:** Postoperative shivering was observed in 13.3% of patients in Ondansetron group and 20% of Meperidine group, significantly lower than the controls (50%). The reduction of core and dermal temperature during the anesthesia and recovery, changes in systolic and diastolic blood pressure and heart rate were similar in all three groups. The incidence of nausea was similar among the three groups of study while vomiting occurred in 6.7% of the Meperidine group and 3.3% of the controls but none in the patients receiving Ondansetron.

**Conclusion:** Ondansetron can effectively reduce post operative shivering.

**Keywords:** General anesthesia, Postoperative shivering, Ondansetron.

## Introduction

Shivering happens frequently after 5 to 60% of surgical operations<sup>1</sup>. Though it occurs as a result of temperature reduction, it may occur in patients with a post-operative normal body temperature<sup>2</sup>. Shivering may be dangerous due to increasing effect of medicines, extension of recovery period, increased oxygen consumption or hemostatic dysfunction especially in patients with a low cardiac reserve<sup>3</sup>. It may also result in hypoxemia<sup>4</sup>.

Several medications have been suggested for the prevention and treatment of shivering. Intravenous use of opioid drugs (Pethidine, Alfentanil, Nalbuphine), non-opioid analgesics (Tramadol), Alpha-2-agonists (Clonidine), respiratory stimulators (Doxapram) or Physostigmine are reported to reduce or treat shivering<sup>5,6</sup>.

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Table 1  
Initial vital signs as mean (SD)

	Normal saline (n=30)	Ondansetron (n=30)	Pethidine (n=30)	p
Age (years)	25.1 (4.2)	26.5 (6.1)	26.0 (5.8)	0.49
Duration of operation (minutes)	34.3 (7.4)	35.6 (7.5)	32.9 (6.1)	0.34
Core body temperature (° C)	37.5 (0.6)	37.5 (0.5)	37.4 (0.4)	0.76
Skin temperature (° C)	36.7 (0.8)	36.7 (0.6)	36.6 (0.5)	0.79
Systolic blood pressure (mmHg)	120.3 (16.1)	114.1 (20.3)	116.3 (16.7)	0.40
Diastolic blood pressure (mmHg)	76.6 (12.9)	73.1 (13.6)	78.3 (11.1)	0.25
Heart rate (beats/minute)	99.7 (16.4)	101.9 (19.2)	94.2 (19.4)	0.25

According to regulator effect of intra-hypothalamic serotonin (5-hydroxy tryptamine) its agonists (Ondansetron) are reported to have the same effect<sup>7</sup>. Contrary to pethidine, Ondansetron may reduce post operative nausea and vomiting (PONV). A medication to reduce both PONV and shivering will be very valuable. This study evaluated the preventive effect of Ondansetron and pethidine on post-operative shivering compared to a control group.

## Patients and Methods

This study was carried out in Alavi University clinic of Ardebil during 2008. The protocol was approved by ethical committee of this University and included female patients undergoing elective gynecologic surgery during a 3 months period. All were in ASA physiologic class I or II. Obese patients (weight >100 kg), patients with fever (body temperature > 38°), endocrine problems or Parkinson disease were excluded as well as patients who received blood, vasodilator or vasoconstrictor medications during the operation. Long duration of the operation (>90 minutes) also resulted in exclusion.

Patients then were randomly selected to receive either 4 mg Ondansetron, 0.4 mg/kg Pethidine or 2cc normal saline (the placebo) 2 minutes before induction of anesthesia. The responsible anesthesiologist was blinded to the drug available in same 2 ml syringes.

Anesthesia was induced by 1 µg/kg fentanyl, 5 mg/kg thiopental and 1 mg/kg succinylcholine and maintained by 1-0.8% Isoflurane in an inspired

mixture of 50% oxygen and 50% N<sub>2</sub>O after intubation. Atracurium was administered to keep muscle relaxation. The patients were mechanically ventilated. Room temperature was set at 20°-22 °C.

Body core and skin temperatures were measured through tympanic membrane and forehead accordingly. Patients were observed for shivering (chills for at least 15 seconds), nausea or vomiting during recovery by a technician blinded to the medication. Patients received pethidine or metoclopramide when necessary.

All data were expressed as the mean ± SD. A chi-squared test was used to compare qualitative variables. A repeated-measures ANOVA and Chi-square tests were used to compare the data before and after each treatment. A P value of 0.05 was considered statistically significant.

## Results

Thirty patients were studied in each group. No significant difference was found in terms of age and initial vital signs between the groups (Table 1). As described in Fig. 1 core body temperature decline in the controls was more than in patients receiving Ondansetron or pethidine but no significant difference was observed between Ondansetron and pethidine groups. Decrease in the skin temperature was not different among three groups (fig. 2).

Systolic and diastolic blood pressure was decreased in all patients during the surgery and came back up during recovery. Heart rate increased after

Fig. 1  
Measured body core temperature in three groups

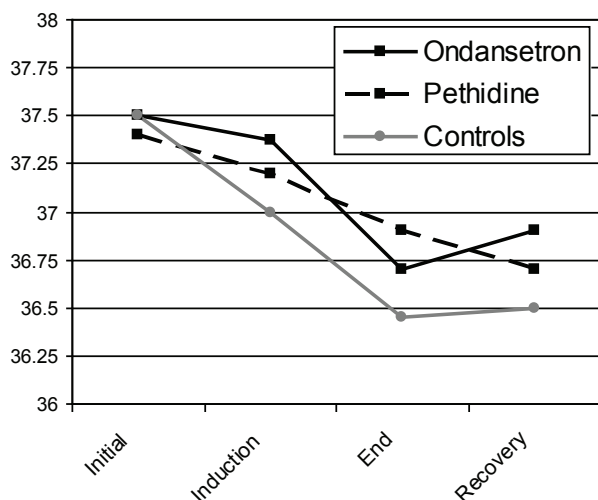
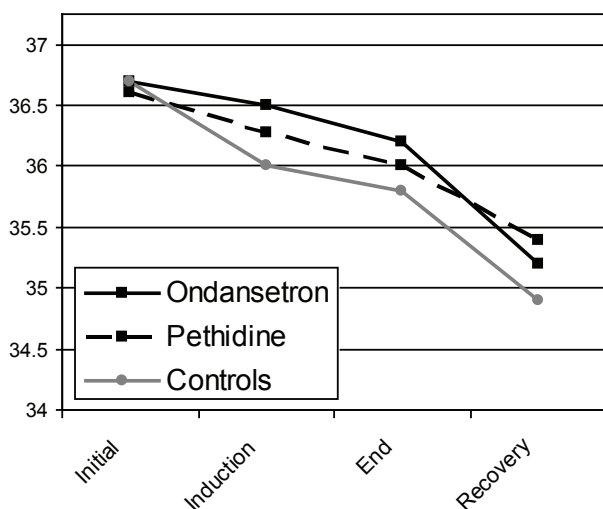


Fig. 2  
Measured skin temperature in three groups



induction of anesthesia and decreased slightly during the operation and recovery. No significant difference was noted among the three groups.

Shivering occurred significantly less in patients receiving Ondansetron or pethidine compared to the controls. Results are shown in Table 2.

Table 2  
Results of post operative observation in three groups

	Normal saline (%)	Ondansetron (%)	Pethidine (%)	P
Shivering	15 (50.0)	4 (13.3)	6 (20.0)	0.003
Nausea	3 (10.0)	3 (10.0)	3 (10.0)	1.00
Vomiting	2 (6.7)	0	1 (3.3)	0.30

## Discussion

General anesthesia accelerates transmission of body core temperature to peripheral tissues and heat regulator mechanisms like the threshold for vasoconstriction became blocked<sup>8</sup>. The first phase of postoperative recovery is influenced by medications yet but along with decrease in their concentration, heat regulator mechanisms re-start functioning in the second phase where a body temperature lower than the set point will result in shivering<sup>9</sup>. Patients will benefit from fine management of shivering which will prevent sympathetic stimulation and excess oxygen use<sup>10</sup>.

The current study reports valuable preventive effect on shivering for Ondansetron and Pethidine compared to controls compatible with some previous reports. Kelsaka et al reported a reduction in the occurrence of shivering after spinal anesthesia from 36% (in controls) to 8% by either Ondansetron or pethidine<sup>4</sup>. Piper et al reported failure of 12.5 mg Dolansetron to decrease this rate which was may be because of its inadequate dosage<sup>4,1</sup>. While Powel et al reported shivering to occur in 57% of patients receiving saline compared to a rate of 33% followed by 4mg Ondansetron and 15% followed by 8 mg Ondansetron<sup>10</sup>. They highlighted the effect of Ondansetron to interfere with heat regulation by a central mechanism.

Similar studies reported adverse effects for other medications. Clonidine may cause hypotension and drowsiness in addition to reducing shivering<sup>12</sup>. Tramadol can reduce shivering but can decrease sweating and vasoconstriction as well<sup>13</sup>. Doxapram as a brain stimulant prevents post operative shivering but has considerable hemodynamic side effects<sup>14</sup>. Physostigmine has significant preventive effects on shivering but increases heart rate and blood pressure and may be harmful in patients with coronary artery disease<sup>6</sup>. It is associated with nausea and vomiting as well. Although pethidine has the minority effect on

cardiovascular system with the dosage used for treating shivering ( $0.3\text{--}0.4\text{ mg/kg}$ )<sup>15</sup>, it may extensively slow down respiration especially if used during the surgery. Results of this study demonstrate the safety of using Ondansetron as well as its efficacy.

In conclusion using Ondansetron instead of pethidine is suggested because of its ability to reduce shivering from 50 to 13.3% in addition to less side effects especially in patients with hemodynamic instability.

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